Triglyceride Glucose-Waist Circumference to Height Ratio Exceeds Commonly Used Anthropometric Markers in Predicting 10-Year Diabetes Risk: the REACTION Research

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Research Article

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Abstract

Purpose

Although Triglyceride glucose-waist-to-height ratio (TyG-WHtR) is an indicator for insulin resistance, the relationship between TyG-WHtR and newly diagnosed diabetes is unclear. The intention of this research is to examine the causative association between TyG-WHtR and new-onset diabetes.

Methods

We conducted a retrospective 10-year cohort study of 10150 Chinese adults. After screening out the unqualified people, the TyG-WHtR level of 8279 participants was calculated in this study, and a multivariate logistic regression model was used to investigate the possibility that it has a connection with diabetes.

Results

Within 10 years, 271 men (3.27%) and 532 women (6.43%) were newly diagnosed with diabetes. Multivariate Cox regression analysis reveals a linear relationship between TyG-WHtR index and newly diagnosed diabetes mellitus (HR=8.889, 95% CI: 4.703 to 16.801, P < 0.001), and TyG-WHtR shows great AUC (0.750, 95% CI: 0.733-0.767). Addionally, TyG-WHtR associated diabetes was shown to be substantially more prevalent in people aged 71 to 80, with a BMI below 24 kg/m^2 and no hypertensive condition (P < 0.05), according to subgroup analysis.

Conclusion

According to the study, TyG-WHtR might be an accuracy indicator of future diabetes risk and outperform other commonly used anthropometric indices.

Introduction

In recent years, diabetes, as one of the most common and prevalent chronic diseases, greatly affects the quality of life and life expectancy of patients and can even lead to disability[1, 2]. The latest report from the International Diabetes Federation reveals that there will be 536.6 million adults aged 20-79 with diabetes in 2021, rising to 783.2 million by 2045[3]. Type 2 diabetes (T2DM) affects more than 90% of diabetics[3–5]. T2DM and its complications are a major cause of disability, functional impairment or premature death, and therefore have enormous social and economic costs[6–8]. As a result, it is critical to improve diabetes prevalence prediction[9, 10].

It is worth noting that a key pathogenic hallmark of T2DM in its early stages is insulin resistance[11]. IR is a significant underlying abnormality that contributes to diabetes[12, 13]. Numerous indices derived from triglyceride glucose (TyG) and anthropometric measurements have been proposed in recent years, including TyG-body mass index (TyG-BMI), TyG-waist circumference (TyG-WC), and TyG-waist to height ratio (TyG-WHtR)[14, 15]. TyG-WHtR is defined as ln[fasting triglycerides (mg/dL) * fasting blood glucose (mg/dL)/2]*WC(cm)/Height(cm) has been posited as a straightforward, low-cost, and convincing surrogate marker for IR and T2DM[15, 16]. Numerous cross-sectional studies have established a link of TyG-WHtR index with IR, T2DM, non-alcoholic fatty liver disease, metabolic syndrome, and hyperuricemia[15–19]. However, no cohort study has established the capability of TyG-WHtR index to anticipate the development of T2DM. For this reason, we compared TyG-WHtR index with other routine anthropometric indices, as well as follow-up data from the earlier REACTION study, in order to see if there was a link between the occurrence of diabetes and this index.

Methods

Study subjects

This study originated from a multi-center national REACTION study initiated by Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine[20-22]. Furthermore, the research sample originated in Luzhou, Sichuan Province. Initial recruitment took place from May to December 2011, with a total of 10,150 participants (all over the age of 40) being recruited.

Exclusion criteria included participants with diabetes mellitus, lack of data on psychological or clinical characteristics, inability to calculate baseline TyG-WHtR values, or missing follow-up data. Eventually, 8279 people were involved in the research.

Baseline assessments (2011)

As part of the REACTION study's baseline examination, all of the study's information and data was collected using standard questionnaires and calibrated devices by trained personnel (e.g., cardiologists, general practitioners, dietitians, and nurses). Each participant provided demographic information (e.g., age, sex, and education level) and medical history information (e.g., smoking habits, drinking habits, used medications, and family medical history). Smokers were divided into three categories based on their history of smoking: none, occasionally, and daily smoke[21]. In addition, participants were classified as none, occasionally, or weekly drink depending on the type, frequency and average quantity of their alcohol consumed[21,22]. Anthropometric indices like BMI (kg/m^2), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) were calculated based on the results of standard measurements of body weight (in kilograms; kg), height (in centimeters; cm), waist circumference (WC) (in centimeters; cm), and hip circumference (in centimeters; cm). After resting for at least 30 minutes in a quiet environment during a physical examination, the arterial blood pressure of the right arm was measured three times continuously, and the average value was taken as the mean arterial blood pressure of the patient. Hypertension was defined as being receiving any antihypertensive medication currently or mean systolic blood pressure (SBP) ≥140 mmHg, mean diastolic blood pressure (DBP) ≥90 mmHg.

TyG-WHtR assessment

TyG-WHtR was determined by calculating for each participant at the baseline examination as ln[fasting triglycerides * fasting glucose /2]*WC/Height[15]. The serum concentrations of TG and FBG are both expressed in mg/dL, WC and Height are both expressed in cm. For the same sample, TyG-WHtR quartiles at baseline were also calculated for the following purposes: Q1(<0.433) (n=2071); Q2(0.434-0.647) (n=2068); Q3(0.648-0.896) (n=2071); Q4(>0.897) (n=2069).

Assessment of sample size of study

In this 10 year retrospective cohort study, we collected detailed interview information directly from 10,150 participants from 2011-2021. Eventually, 649 individuals with diabetes at baseline and 1222 with missing follow-up data were omitted from the study for the purpose of this study's' objectives and analyses, resulting in a sample size of 8279 participants.

Statistical analysis

Baseline clinical characteristics were compared for target participants using standard descriptive statistics across the baseline TyG-WHtR quartiles. The Kruskal-Wallis test was used to determine whether the variables were normally distributed, where differences in normally distributed continuous variables were assessed by one-way analysis of variance (ANOVA) and differences in non-normally distributed variables were assessed by the Wilcoxon rank sum test. The Mean-Whitney test was used to determine whether there was a statistically significant difference in means between each pair of groups. The association between the risk of developing diabetes and TyG-WHtR quartiles was analyzed

using Kaplan–Meier curves and log-rank test. Using the receiver operating characteristic curves (ROC curves), we explored the predicted accuracy of the TyG-WHtR index. All statistical analyses were conducted by SPSS (version 26.0).

Results

10-year T2DM incidence

From 2011 to 2021, a total of 8279 people were enrolled in the study, including 2715 males and 5564 females. During this period, there were 803 newly diagnosed diabetes patients, and the incidence of diabetes was 9.7%.

Quartiles of TyG-WHtR index in the study participants

Baseline clinical and biochemical characteristics of participants by TyG-WHtR index quartiles are presented in Table 1. Through data analysis, we revealed a positive association between TyG-WHtR index quartiles and risk factors of diabetes, such as age, BMI, WC, SBP, DBP, fasting blood glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, current smoking, alcohol consumption, and high prevalence of hypertension and coronary heart disease (all $p < 0.001$); negatively correlated with high-density lipoprotein cholesterol ($p < 0.001$). However, no powerful correlations were found between TyG-WHtR index quartiles and tea or coffee consumption.

Table 1 Characteristics according to TyG-WHtR index quartile

	TyG-WHtR				
Baseline characteristics	Quartile 1 (n=2070)	Quartile 2 (n=2069)	Quartile 3 (n=2070)	Quartile 4 (n=2070)	P-value
Diabetes 10-year incidence, n(%)	50(2.4%)	91(4.4%)	210(10.1%)	452(21.8%)	<0.001†
age	54.44± 9.74	57.41±10.25	59.14±9.59	61.32±9.72	<0.001*†
Male sex,n(%)	682(32.9%)	718(34.7%)	703(34.0%)	605(29.2%)	<0.01
Weight,kg	52.75±7.47	57.40±7.99	61.31±9.06	65.26±10.18	<0.001*†
BMI,kg/m^2	20.85±2.32	22.93±2.24	24.63±2.42	26.79±2.92	<0.001*†
WC,cm	76.12±8.31	80.67±8.29	84.49±8.20	89.40±8.25	<0.001*†
Hipline,cm	87.41±6.74	92.34±5.80	95.67±5.84	99.98±7.17	<0.001*†
WHR	0.83±0.07	0.87±0.06	0.90±0.06	0.93±0.06	<0.001*†
WHtR	0.45±0.03	0.51±0.03	0.54±0.03	0.59±0.04	<0.001*†
SBP,mmHg	115±17.46	122±18.40	127±19.08	133±18.84	<0.001*†
DBP,mmHg	72±9.81	76±10.31	78±10.96	80±10.63	<0.001*†
TC,mmol/L	4.19±1.06	4.50±1.08	4.70±1.07	4.95±1.18	<0.001*†
TG,mmol/L	0.89±0.34	1.22±0.50	1.60±0.79	2.61±1.97	<0.001*†
HDL-cmmol/L	1.37±0.38	1.28±0.34	1.23±0.32	1.14±0.30	<0.001*†
LDL-c,mmol/L	2.27±0.74	2.59±0.80	2.71±0.80	2.74±0.84	<0.001*†
FBG,mmol/L	5.25±0.59	5.42±0.73	5.64±1.06	6.12±1.60	<0.001*†
HbA1c,%	5.75±0.55	5.84±0.59	5.97±0.75	6.27±1.08	<0.001*†
ALT,mmol/L	11.18(11.19,11.98)	13.60(113.18,14.02)	15.41(14.96,15.86)	18.84(18.24,19.45)	<0.001*†
AST,mmol/L	19.55(19.10,20.01)	20.54(20.12,20.95)	21.64(21.12,22.16)	23.77(23.16,24.38)	<0.001*†
TyG	8.15±0.37	8.49±0.39	8.78±0.43	9.25±0.59	<0.001*†
Family history of diabetes, n(%)	408(19.7%)	357(17.3)	372(18.0%)	318(15.4%)	<0.01
Hypertension	124(6.0%)	246(11.9%)	366(17.7%)	554(26.8%)	<0.001*
Coronary disease	45(2.2%)	39(1.9%)	63(3.0%)	99(4.8%)	<0.001*
Smoking					0.05

Never	1740	1750	1770	1810	
Former	54	53	57	50	
Current	276	266	243	210	
Drinking	605(29.3%)	627(30.3%)	504(29.2%)	537(26.0%)	<0.01
Never	1465	1442	1466	1533	
Fomer	451	451	424	364	
Current	154	176	180	173	
Coffee	150(7.2%)	141(6.8%)	144(7.0%)	130(6.3%)	0.66
tea	1071(51.7%)	1121(54.2%)	1101(53.2%)	1051(50.8%)	0.42

The values were expressed as mean (standard deviation), medians (quartile interval), or n (%).

Abbreviations: FPG fasting plasma glucose, TG triglyceride, TC total cholesterol, LDL-C low-density lipid cholesterol, HDL-c high-density lipid cholesterol, ALT alanine aminotransferase, AST aspartate aminotransferase.

* $p < 0.001$.

† Q2/Q3/Q4 vs Q1; $p < 0.001$

all *p* values for TyG-WHtR index quartiles were determined by using an analysis of variance with Bonferroni post hoc method.

TyG-WhtR and diabetes incidence over 10 years

The analysis revealed a total of 803 patients with newly diagnosed diabetes during the 10-year follow-up period, with an incidence of n = 44 (2.1%), n = 89 (4.3%), n = 184 (8.9%), n = 486 (23.5%) in the baseline TyG-WHtR quartiles (Table 1). It can be found that with the increase of TyG-WHtR index, the prevalence of diabetes also increased (5.5%, 11.1%, 22.9% and 60.5%, respectively). To adjust for other residual confounders, we performed a conditional logistic regression analysis with a binary outcome of diabetes in relation to TyG-WHtR index (Table 2). Diabetes risk was higher in the second (1.044, 95% CI 0.718–1.519), third (1.613, 95% CI 1.085–2.400), and fourth (1.898, 95% CI 1.127–3.196) quartiles of TyG-WHtR index than in the first ($p < 0.001$). There were a number of factors taken into account in the analysis, including age; gender; WHR; WHtR; BMI; SBP; DBP; FBG; HbA1c; HDL; and LDL; family history of diabetes; cigarette smoking; drinking coffee; tea; coronary disease; and hypertension. Finally, diabetes risk increased significantly and steadily as the TyG-WHtR index quartile increased.

Table2 Correlation between TyG-WHtR index and diabetes risk

	Per 1-unit increase in TyG-WHtR	Q1	Q2	Q3	Q4
Modle 1	3.554(3.185,3.965)	Ref	1.056(0.726,1.536)	1.639(1.103,2.437)	1.930(1.147,3.246)
Modle 2	3.571(3.191,3.996)	Ref	1.044(0.718,1.519)	1.613(1.085,2.400)	1.898(1.127,3.196)
Modle 3	8.889(4.703,16.801)	Ref	1.099(0.738,1.636)	1.655(1.067,2.568)	1.851(1.030,3.324)

Modle 1 crude

Modle 2 adjusted for age and sex

Modle 3 adjusted for age, sex, WHR, WHtR, BMI, SBP, DBP, FBG, HbA1c, ALT, AST, TG, HDL, LDL, family history of diabetes, smoke, drink, coffee, tea, coronary disease, and hypertension.

As illustrated in Figure.1，survival statistics analysis were performed using Kaplan–Meier survival curve with log rank test, and the results indicated that the aggregate prevalence of diabetes was significantly different among the four TyG-WHtR index groups (P< 0.001) . Increases in the TyG-WHtR index were significantly associated with an increased risk of developing diabetes.

Subgroups analysis

As previously stated, TyG-WHtR is an indicator that can more accurately reflect the body's metabolic state. In order to explore the effect of additional risk factors on the correlation between TyG-WHtR index and future diabetes risk, subgroup comparisons were conducted using the previously mentioned stratification factors. Table 3 summarizes the different interactions for the different between-study subgroup analysis. TyG-WHtR index and diabetes risk were found to have additive interactions in age, BMI, as well as hypertension ($P < 0.05$). Participants between the ages of 71 and 80, with BMI < 24 kg/m^2, and without hypertension were found to have the strongest interrelations. However, the outcomes of this survey did not show significant interactions among gender, family history of diabetes, coronary disease, smoking, drinking, or tea consumption.

Table 3 Association of TyG-WHtR with diabetes risk in subgroup analysis

Subgroup	No. of participants	Unadjusted HR (95%CI)	Adjusted HR (95%CI)	P-value for interaction
Gender				0.577
Male	2708	3.117(2.645,3.674)	18.869(6.359,55.989)	
Female	5571	2.948(2.655,3.274)	10.833(5.545,21.163)	
Age(years)				<0.001
<51	1963	4.079(3.184,5.224)	7.120(1.907,26.574)	
51-60	2802	2.914(2.512,3.381)	27.324(9.172,81.405)	
61-70	2305	2.717(2.346,3.147)	9.031(3.613,22.574)	
71-80	1031	2.541(1.955,3.302)	59.461(7.963,443.980)	
>80	178	2.058(0.764,5.547)	0.000(0.000,5.664E+9)	
BMI(kg/m^2)				0.002
<24	4516	3.985(3.355,4.734)	37.073(13.188,104.221)	
≥ 24, < 28	2891	3.071(2.601,3.626)	15.118(6.092,37.519)	
≥28	872	2.294(1.803,2.919)	2.913(0.860,9.871)	
Family history of diabetes				0.493
No	6824	3.020(2.735,3.335)	18.100(8.925,36.706)	
Yes	1455	2.807(2.329,3.383)	5.885(2.043,16.950)	
Hypertension				0.033
No	6989	3.029(2.725,3.367)	13.813(7.067,26.997)	
Yes	1290	2.472(2.075,2.945)	7.613(2.659,21.796)	
Coronary disease				0.403
No				
Yes	8033	2.979(2.723,3.259)	11.961(6.726,21.271)	
	246	2.440(1.591,3.741)	7.037(0.431,114.794)	
Smoking				0.435
None	7070	2.931(2.667,3.220)	11.223(6.210,20.282)	
Occasionally	214	3.587(1.902,6.765)	6.361(0.058,701.821)	
Daily	995	3.270(2.503,4.273)	35.972(4.527,285.805)	
Drinking				0.106
none	5906	2.841(2.566,3.146)	9.843(5.086,19.049)	
Occasionally	1690	3.485(2.829,4.293)	37.413(9.849,142.122)	
Weekly	683	3.341(2.403,4.647)	7.447(1.477,37.537)	

Coffee				0.998
No	7714	2.971(2.712,3.256)	11.889(6.642,21.279)	
Yes	565	2.999(2.178,4.129)	23.784(2.280,248.092)	
Tea				0.176
No	3935	2.786(2.448,3.171)	8.470(3.830,18.735)	
Occasionally	2501	3.058(2.617,3.574)	28.691(9.374,87.817)	
Used to often	86	2.049(0.704,5.962)	0.000(0.000,8.466E+22)	
Often	1757	3.307(2.741,3.990)	6.135(1.795,20.970)	

Adjusted for gender, age, weight, FPG, HbA1c, ALT, AST, TG, HDL-C, SBP. DBP, WHR, WHtR, BMI, smoke, drink, coffee, tea, coronary disease, hypertension and family history of diabetes.

The ability of TyG-WHtR index to predict new-onset diabetes

Receiver operating characteristic (ROC) curves were used to assess the accuracy of TyG-WHtR index in predicting newly diagnosed diabetes (Fig. 2). FBG, BMI, WC, WHtR, TyG, TyG-BMI, TyG-WC and TyG-WHtR had an area under the curve (AUC) of 0.838 (0.822-0.853), 0.649(0.629-0.668), 0.674(0.655-0.693), 0.679 (0.660,0.698), 0.752 (0.735-0.770), 0.723(0.705-0.741), 0.748(0.731-0.765) and 0.750 (0.733-0.767) for predicting new-onset diabetes, respectively. Compared to BMI, WC, WHtR, TyG-BMI and TyG-WC, the AUC of TyG-WhtR was considerably higher ($P < 0.0001$). However, FPG and TyG performed better than TyG-WhtR in this research when it came to predicting new-onset diabetes. With a 72.98 % sensitivity and 65.10 % specificity, the best cut-off value for TyG-WhtR was 4.746.

Discussion

The incidence of diabetes is expanding at an astonishing speed at present[10]. It was estimated that 10.5% of adults aged 20–79 had diabetes (uncertainty interval: 8.3%–12.0%), with 10.8% of men and 10.2% of women having the condition[3]. The increase in the global burden of diabetes is accompanied by an increase in medical expenditures to treat this disease, which will significantly increase the economic burden of society. Therefore, it is critical to enhance preventive care as well as screening of high-risk groups[23]. Insulin resistance and the failure of beta cells are hallmarks of T2DM[24]. The glucose-clamp technique, which was pioneered by DeFronzo, is widely regarded as the gold standard for quantifying insulin resistance[25]. Unfortunately, this method is time-consuming and expensive, so IR is typically measured by less invasive methods, such as TyG index and obesity-related metrics including BMI, WC, and WHtR[26,27]. Lim, Jinsook et al. combined the TyG and WHtR indices for the first time and demonstrated that TyG-WHtR outperformed TyG index alone in assessing insulin resistance[15].

Previous studies have shown a connection between diabetes mellitus and TyG-WHtR index. A cross-study of 24,215 normal-weight Chinese elderly individuals from August to December 2019 in Shenzhen found that a higher TyG-WHtR index (AUC: 0.760, 95 % CI 0.749-0.771) was remarkably linked with an increased incidence of diabetes, though it was less than TyG index (AUC: 0.818, 95% CI 0.810–0.825)[16]. Which is consistent with our study. On the other hand, we find some evidence linking TyG-WHtR to metabolic syndrome. A study comparing IR indices in metabolic syndrome discovered that TyG-WHtR had the highest AUC for metabolic syndrome identification (AUC: 0.863, 95%CI: 0.828-0.892), significantly higher than TyG index (AUC: 0.796, 95% CI: 0.757-0.831)[19]. Another cross-sectional study involving non-diabetic participants aged 18 and up found that all IR indexes studied can distinguish individuals with metabolic syndrome from those who are healthy. TyG had the highest area under the curve AUC:0.888, 95% CI: 0.862-0.915), while TyG-WHtR index(AUC:0.847, 95% CI: 0.818-0.876)[28]. It can be found that diabetes and metabolic syndrome can be

accurately predicted by TyG-WHtR index. Additionally, the index can predict non-alcoholic fatty liver, too. Malek, Mojtaba et al. discovered that TyG-WHtR had the highest AUC for detecting NAFLD (0.783, P < 0.001), outperforming TyG (AUC: 0.647, P = 0.002) and other indexes in ROC analysis. Additionally, it was confirmed that the TyG-WHtR index, which combines TyG and obesity parameters, is more effective at detecting hepatic steatosis than TyG alone[29].

A longitudinal, multi-center representative cohort data was used to examine the connection between TyG-WHtR index and diabetes in this study. New-onset diabetes were found to be linked to a high TyG-WHtR index, even after correcting for potential related confounders, such as coronary heart disease and hypertension risk factors. In addition, these conclusions were shown in analyses of age, BMI, and hypertension subgroups, highlighting the consistency of this connection even further. As previously reported , in Asian countries such as China and India, where the prevalence of T2DM is characterized by a lower BMI at onset, our study confirms that people with a BMI < 24 kg/m^2 are at a much higher risk of having T2DM than those who are obese or overweight[30,31]. Observational studies should be construed with caution, but this large national survey with 10,150 participants discovered that a higher TyG-WHtR score might be a considerable indicator of forthcoming diabetes cases[32].

A few advantages came out of this research. Using TyG-WHtR as a marker for predicting diabetes is the main advantage of this study, which assesses the risk of developing diabetes. Additionally, the study was followed for a period of up to 10 years, making it more relevant. An additional step to ensure the accuracy and avoid the contingency of the data was taken by using TyG-WHtR index was analyzed as a continuous variable and as a categorical variable (quartiles), which was then followed by performing a trend test and a sensitivity analysis. However, the present study has a limitation in that it only included a sample of adults in southwest China who were 40 years old or older, failing to cover all regions in China. Secondly, the parameters used to calculate TyG-WHtR were collected throughout the study, and TyG-WHtR changes were not monitored during follow-up. As a result, additional investigation is necessary to determine the clinical value of TyG-WHtR in patients with T2DM.

Conclusions

Eventually, using a longitudinal multi-center representative cohort data, we demonstrated a substantial rise in diabetes risk as TyG-WHtR index grew. Because of observation-based study design has internal limitations, this study does not imply a causal relationship. Our findings indicate that TyG-WHtR index, a proxy marker for insulin resistance, is an independent and reliable indicator of risk for the development of diabetes.

Declarations

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Conflict of Interest

All the authors declare that there is no conflict of interest.

Author Contributions

All the authors contributed to the discussion and manuscript preparation. Jie Lin and Hang Li contributed equally to this work, who organized data collaboration, interpreted statistical analyses, and wrote the Article; Yahui Qin and Xin Xiang checked multiple-site data, Qin Wan designed the study. All authors read and approved the final manuscript.

Ethics approval

The research adhered to the ethical standards of the Helsinki Declaration (1975) and the research protocol was reviewed and approved by the ethics committee of the Affiliated Hospital of Southwest Medical University.

Consent to participate

Everyone who took part in this research gave their explicit, verbal, and/or written consent before participating. Throughout the data collection and analysis processes, the privacy of participants was protected.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of all data.

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Figures

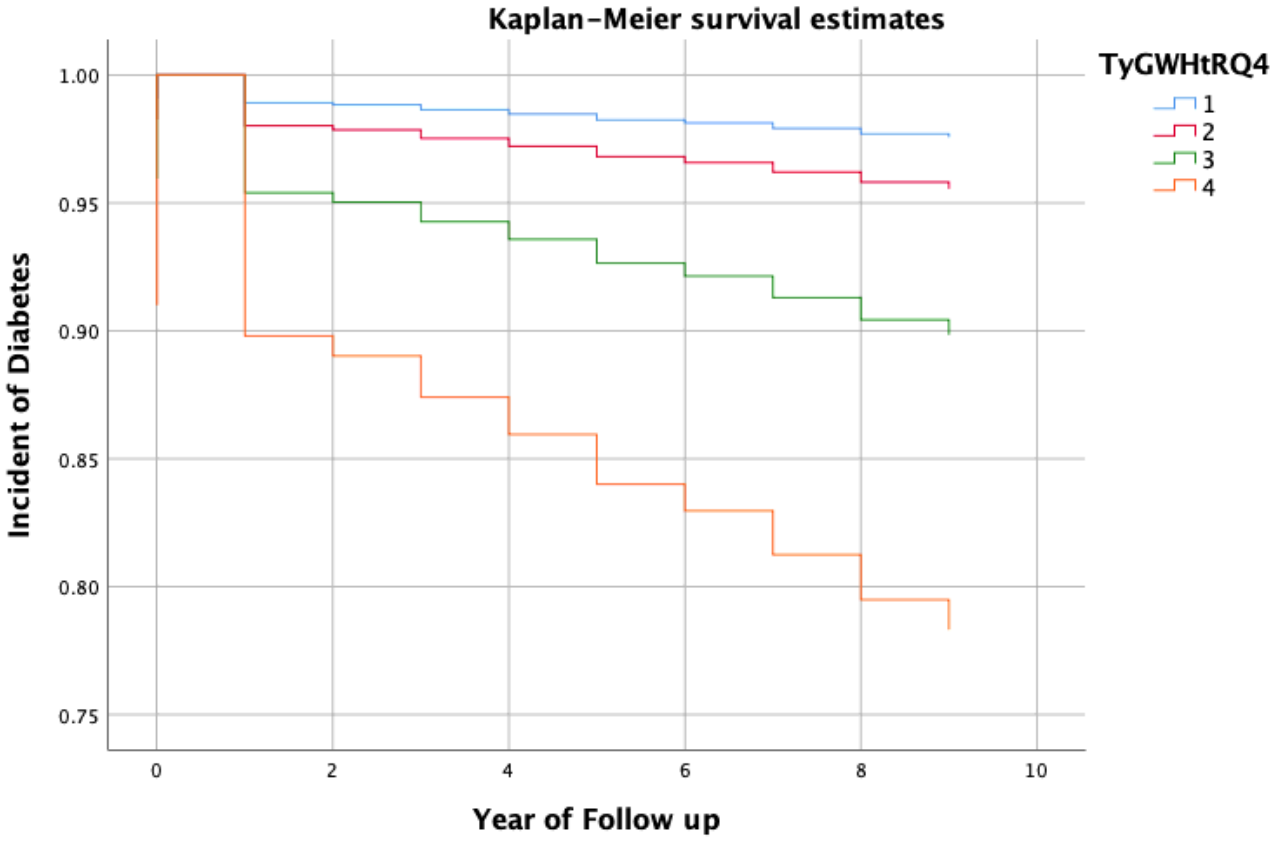

Figure 1

Kaplan-Meier estimates of the risk of developing diabetes stratified by quartiles of TyG-WHtR index (P < 0.001)

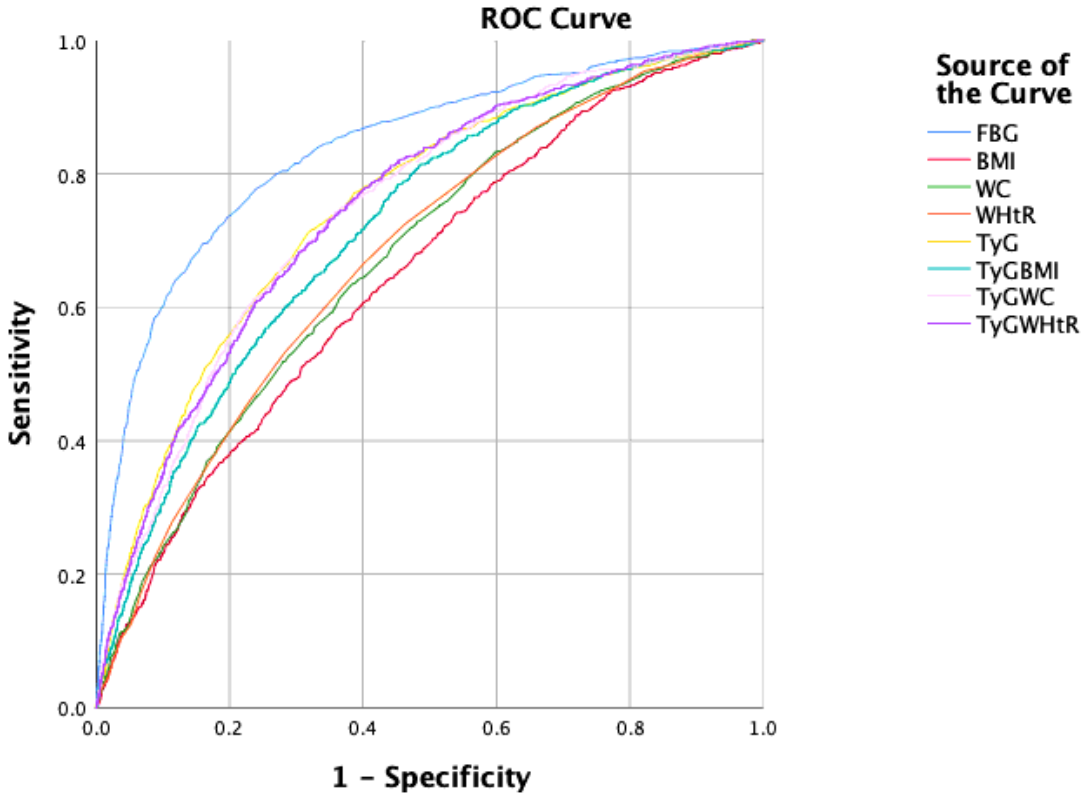

Figure 2

ROC analysis is used to anticipate diabetes